A Stochastic Approach to Modeling, Parameter Estimation, and Simulation of Enzymatic Reactions

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Models that can accurately simulate and describe enzyme-inhibitor interactions can be extremely valuable. For instance, in proteinase-catalyzed destruction of connective tissues, they can be used to predict the conditions favoring the skew of proteinase-antiproteinase balance in the direction of proteolysis. This is critical in order to improve upon present day therapeutic interventions for controlling inflammatory tissue injury and tumor invasiveness.

The traditional approach to the analysis of the kinetics of enzymatically catalyzed reactions assumes uniform and homogeneous concentrations of reactants and products. If these assumptions are applied to proteinase-catalyzed destruction of connective tissues by inflammatory cells, the ensuing analysis is inaccurate [1]. The challenges in understanding the kinetics of such processes arise from the fact that the sites of reaction are no longer uniformly and continuously distributed but rather are discrete.

In this paper we develop in these models that can describe the discrete events occurring at localized environments associated with cell-mediated proteolysis. These models accurately simulate time evolutions of chemical reactions in nonisotropic environments. The starting point is the available theory of stochastic processes for chemical reactions [3], which considers time evolutions of spatially homogeneous mixtures of chemically reacting molecules. The new models are distinctly different from the ones employed in conventional chemical kinetics that are based on coupled differential equations. Since the resulting stochastic models involve many important parameters of biological interest, we provide methods to predict and estimate the unknowns of interest, namely the reaction constants and the amount of molecules of the reactants, from the observations. The estimation of the reaction constants has already been addressed in [2] under the assumption that the trajectories in the amount of molecules are known which is very difficult to hold in practice. Our only assumption rests in considering that a limited number of discrete-time measurements is available. Computer simulations show that the proposed models and estimation methods are adequate to represent this type of systems.

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References

1. E. J. Campbell, M. A. Campbell, S. S. Boukedes, C. A. Owen, "Quantum proteolysis by neutrophils: implications for pulmonary emphysema in α_1-antitrypsin deficiency," The Journal of Clinical Investigation, vol. 104 (3), 1999.
2. M. A. Gibson, "Computational methods for stochastic biological systems," Ph. D. thesis, California Institute of Technology, Pasadena CA, 2000.
3. D. T. Gillespie, "A general method for numerically simulating the stochastic time evolution of coupled chemical reactions," Journal of Computational Physics, vol. 22, pp. 403-434, 1976.